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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/552,087
Filing Date: April 21, 2000
Appellant(s): BYRUM, JOSEPH R.

Joseph R. Byrum
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 5/25/07 appealing from the Office action mailed 10/30/06.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

The related appeals and judicial proceedings known to the examiner are identical to those set forth in the Appeal Brief at page 2.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows: There are two different rejections under 112 1st paragraph. One is a lack of enablement which follows the lack of utility rejection, a so-called follow on rejection. In addition, however, there is also a lack of enablement rejection which discusses reasons why the one would not be able to make and use the claimed subject matter which is separate from the "lack of utility" enablement rejection.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Alignment of instant SEQ ID NO: 1 with a POL3-like gene from Phaseolus coccineus.

GenBank Record having Accession AF147259 (13 August 1999)

Pietrzkowski et al. Experimental Cell Research, Vol. 193, pages 283-290 (1991)

Chan et al. Plant Molecular Biology, Vol. 46, pages 131-141 (2001)

Omilli et al. Molecular and Cellular Biology, June 1986, pages 1875-1885

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

Claims 3, 5-7, 9-10, and 12-20 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

Rejected claims 3, 5-7, and 9-10 are drawn to plant host cells and transgenic plants that comprise a construct having a promoter, wherein the promoter nucleic acid molecule comprises SEQ ID NO: 1 or a complement thereof linked to a structural nucleic acid molecule and a 3' non-translated sequence that functions in said cell to cause termination of transcription.

Claims 12-20 are drawn to substantially purified nucleic acid molecules that comprise instant SEQ ID NO: 1 or a nucleic acid sequence that is related to instant SEQ ID NO: 1 by a percent identity. Thus the claims encompass SEQ ID NO: 1 and many, many variants of the sequence.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use.

A well-established utility is defined as a specific, substantial and credible utility which is well known, immediately apparent or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. The instant host cells and transgenic plants do not have a well established utility because the art does not teach any utility for the instantly claimed host cells and transgenic plants that is specific, substantial, and credible.

The specification discloses a number of general utilities for the nucleic acids disclosed herein. For example, the specification generally discloses that these nucleic acids are useful in genetic mapping studies (p. 35), physical mapping (p. 43), contig mapping (p. 46), comparative mapping (p. 49-56), the identification of polymorphisms (p. 49-56), monitoring expression (p. 56), locating regions of identity by descent between individuals (p. 58), isolating clones (p. 59), microarray based methods (p. 60), direct site mutagenesis (p. 60), transformation (p. 62-80), in cosuppression (p. 80), to reduce gene function (p. 82), and as antibodies (p. 83). None of these asserted utilities are specific because the disclosed uses of the nucleic acids are generally applicable to any nucleic acid and therefore are not particular to the nucleic acid sequences being claimed.

The instant specification herein discusses transformation of cells and plants in general (p. 62-80), but does not discuss these methodologies with regard to SEQ ID NO: 1 in particular.

The specification in table 1 sets forth that the protein encoded by instant SEQ ID NO: 1 has 50% identity with a putative POL3 protein from Arabidopsis, but the specification does not assert a utility for SEQ ID NO: 1 or the protein encoded by SEQ ID NO: 1 based on this homology. The fact that SEQ ID NO: 1 encodes a polypeptide that has homology to a "putative" protein suggests that the functionality of the Arabidopsis protein has not been confirmed. Thus, further experimentation would be required to reasonably confirm the identity of the protein both for Arabidopsis and for Glycine max proteins. Beyond that, further experimentation would still be required to establish a real world utility for such a protein.

The specification teaches that nucleic acid molecules and fragments thereof may be employed as genetic markers (p. 35 and following). Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities, and this is particularly the case with regard to correlation with phenotypic traits or genetic mapping of phenotypic traits. The specification has not demonstrated that instant SEQ ID NO: 1 is related to any particular phenotypic trait, nor has it provided any specific suggestion or discussion of any trait SEQ ID NO: 1 might be related to.

The specification suggests that the claimed nucleic acids may be used in transformation to express any polypeptide that is encoded by the transformed sequence (p. 62 and following). No specific function of the polypeptide encoded by SEQ ID NO: 1 has been provided. The specification has provided no information as to what effect the expression of SEQ ID NO: 1 in a transgenic plant cell or plant would have on the plant. The suggestion that instant SEQ ID NO: 1 can be used to transform plants is an invitation to do further research to determine what effect the

sequence might have on plants, or what product is produced upon expression of the encoded polypeptide, if one is encoded.

Claims 3, 5-6, 7, 9, and 10, are drawn to transformed plant cells and transgenic plants that have a construct which contains instant SEQ ID NO: 1 or its complement as "an exogenous promoter region" that functions in a plant cell to cause the production of an mRNA molecule. Thus, these claims suggest that SEQ ID NO: 1 is being included in the host cells and transgenic plants of claim 3, 5, and 6 for its functionality as a "promoter." This is not considered a substantial utility because further experimentation would be required to reasonably confirm that SEQ ID NO: 1, or its complement, or fragments of either would function as a promoter as required by the claims.

The specification does not provide any guidance as to the use of SEQ ID NO: 1, its complement or fragments thereof as promoters. In order to use the claimed invention, one would first have to confirm that either SEQ ID NO: 1 or its complement is in fact a promoter, then determine which fragments are also promoters. There is no evidence on the record to point one to the conclusion that the instantly disclosed sequence is or contains a promoter rather than an intron or a coding sequence, both of which are also suggested as possibilities for SEQ ID NO: 1. The specification teaches at page 101 that instant SEQ ID NO: 1 has 50% identity with a gene encoding a putative POL3 protein from Arabidopsis thaliana. The examiner was not able to confirm this result with a sequence search. However, a sequence search did reveal a sequence disclosed post-filing of this application that has 40.5% identity with instant SEQ ID NO: 1 to a POL3-like gene from *Phaseolus coccineus*, and that this identity occurs over a portion of the gene that is within the portion encoding the translated protein (see attached alignment and further

explanation). The sequence search did not identify any sequences with which instant SEQ ID NO: 1 had identity to any promoter.

Even if one were to assume that SEQ ID NO: 1 contained or was a "promoter," one would have to determine the type of promotion conferred by SEQ ID NO: 1, that is, one would have to determine if the promotion is tissue specific or constitutive, for example, or if it is an inducible promoter, and under what circumstances it is induced or repressed in order to make use of the claimed host cells or plants. Without knowing the conditions under which the promoter could be used one would not know how to use the invention. Each of these determinations is highly unpredictable, from the determination as to whether or not SEQ ID NO: 1 or its complement is in fact a promoter to the determination of the type of promoter it may be to the determination of fragments of the promoter that confer promotion activity. There has been no specific assertion that in fact SEQ ID NO: 1 is a promoter, aside from the claims. The specification generally suggests that all of the sequences disclosed in the application might be promoter molecules (p. 16), but the specification also generally suggests that all of these molecules may comprise introns and coding sequences (p. 24 and 29). Thus, the teachings of the specification themselves, by providing a number of different potential and conflicting descriptions of SEQ ID NO: 1 provide reason to question whether the sequence in fact comprises a promoter, a partial promoter, an exon or an intron or some combination of these. The specification has not provided any further guidance as to the use of SEQ ID NO: 1 as a promoter or its use in any other capacity. Thus, it is left to one attempting to make and use the claimed products to determine which instant SEQ ID NO: 1 actually is and how it can be used within the constructs claimed. Even given the choice between the suggestion that SEQ ID NO: 1 comprises

a promoter or a partial promoter, the specification does not provide any guidance or suggestion as to which is the case for SEQ ID NO: 1. This is an important distinction since the entire functioning of a promoter is entirely sequence specific. For example, if SEQ ID NO: 1 contained only a partial promoter, it is highly unpredictable as to whether or not that partial promoter would function to promote production of an mRNA or which part of SEQ ID NO: 1 is in fact the "promoting" part since one cannot simply look at SEQ ID NO: 1 and identify these regions by any disclosed sequence characteristics, and since the function of a promoter is highly sequence specific. Or, if SEQ ID NO: 1 contains a regulatory element, it is highly unpredictable how that element would function in view of the fact that there are hundreds of possible regulatory functions known, and there is no known way to predict if one of these is attributable to instant SEQ ID NO: 1. The instant specification provides a seven page listing of possible functions that any potential regulatory element contained within the disclosed sequences might have (pages 17-23). Each function would warrant use in a different type of system for expression under different circumstances to achieve an effect specific to the regulatory element. For example, the specification makes reference to oxygen responsive elements, light regulatory elements, and elements responsive to gibberellin. In order to make the claimed invention, one would have to undertake enormous amounts of experimentation to discover if in fact SEQ ID NO: 1 is a promoter or comprises a promoter or a regulatory element, as suggested by the claims and also suggested by the specification, or if SEQ ID NO: 1 contains a structural gene as also suggested by the specification, or if SEQ ID NO: 1 comprises an intron or an intron/exon boundary as also suggested by the specification.

Considering then, the state of the prior art, instant SEQ ID NO: 1 is a novel sequence. A sequence search by the examiner in a variety of nucleic acid databases did not identify any sequence in the prior art with greater than 29% identity over the full length of SEQ ID NO: 1. For example, GenBank AF147259 (13 August 1999) provides the sequence of an A. thaliana BAC, and nucleotides 46185-46519 of this sequence have 29% identity with instant SEQ ID NO: 1. This however is an uncharacterized portion of nucleic acid, and even if the homology were exact would not provide any further guidance as to whether instant SEQ ID NO: 1 contains a promoter or promoter elements, or an intron, or a coding sequence.

Given all of these considerations, the use of instant SEQ ID NO: 1 as a promoter is not a specific or substantial utility since further experimentation would be required to confirm that in fact SEQ ID NO: 1 has the ability to cause the production of an mRNA molecule and the conditions under which such activity occurs. Thus, no utility has been described for the transformed plant cells and transgenic plants comprising SEQ ID NO: 1 wherein SEQ ID NO: 1 is within the construct as a promoter.

It has not been demonstrated that SEQ ID NO: 1 has any utility as a marker for a specific phenotypic trait. After further research, a specific and substantial credible utility might be found for the claimed cells and plants. This further characterization, however, is part of the act of invention and until it has been undertaken, Appellant's invention is incomplete.

In the instant case, the specification has provided a wide variety of general guidance that any of the over twenty thousand disclosed sequences may be promoters, coding sequences or introns. The specification has suggested that any of these may be useful for a wide variety of purposes, some of which conflict with one another. For example, if SEQ ID NO: 1 is a

promoter or contains a promoter, it is not a coding portion of a gene. If SEQ ID NO: 1 is a promoter, than it would not be an expressed sequence so it could not be used to monitor expression of genes via a microarray (as suggested on page 56). The instant claims are limited to instant SEQ ID NO: 1, and some of these require that SEQ ID NO: 1 is within an exogenous promoter region. However, these claims do not remove the entirely general disclosure of the specification which suggests a wide variety of functions and uses for all of the disclosed sequences, but no specific and substantial utility for any one sequence, including instant SEQ ID NO: 1.

The facts in this case are very similar to the facts in In re Fisher (CAFC, 04-1465, 9/7/2005). In both applications, a general disclosure is given to support the disclosure of a nucleic acid whose particular function is not disclosed. The court found that none of the utilities generally suggested for the claimed nucleic acids and compositions in the Fisher case (as a molecular marker, measuring expression, source for primers, identifying polymorphisms, isolating primers, controlling protein expression, or searching for genes in other plants) was enough to overcome the utility requirement. The instant case is similar in that the specification provides merely hypothetical possibilities for uses for the claimed invention. The court has ruled that these are not sufficient to provide a specific and substantial utility to the claimed invention.

As noted by Brenner v. Manson, 383 U.S. 519, 535-536 (1996), and quoted in In re Fisher, "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing...a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Neither the specification as filed nor any art of record discloses or suggests any property or

activity for the claimed cells and plants such that another non-asserted utility would be well established for the compounds.

For these reasons, the claimed nucleic acids, host cells and transgenic plants are not supported by either a specific and substantial asserted utility or a well established utility. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed.

Claim Rejections - 35 USC § 112, 1st paragraph

Claims 3, 5-7, 9-10, and 12-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidenced in the discussions *supra*, each of these factors have been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to use the instant invention.

Claim Rejections - 35 USC § 112

Claims 3, 5, 6, 7, 9, 12, 13, 14, 15, 16, 17, 18, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Independent claim 3 is drawn to a transformed plant cell having a nucleic acid molecule which comprises "(A) an exogenous promoter region which functions in said cell to cause the production of a mRNA molecule, wherein said promoter nucleic acid molecule comprises SEQ ID NO: 1 or the complement thereof", wherein (A) is linked to a structural nucleic acid molecule encoding a polypeptide or protein and a 3' non-translated sequence that functions in said cell. Dependent claims 5 and 6 merely recite that the plant cell is a monocot or dicot plant cell. Thus, the nature of the invention in this case is that the claimed invention is to a plant cell comprising an exogenous promoter- and that promoter comprises therein SEQ ID NO: 1.

Independent claim 7 is drawn to a transformed plant having a nucleic acid molecule which comprises "(A) an exogenous promoter region which functions in said cell to cause the production of a mRNA molecule, wherein said promoter nucleic acid molecule comprises SEQ ID NO: 1 or the complement thereof", wherein (A) is linked to a structural nucleic acid molecule encoding a polypeptide or protein and a 3' non-translated sequence that functions in said cell. Dependent claims 9 and 10 merely recite that the plant cell is a monocot or dicot plant cell. Thus, the nature of the invention in this case is that the claimed invention is to a plant cell comprising an exogenous promoter- and that promoter comprises therein SEQ ID NO: 1.

Regarding the scope of the claims, the remand by the board suggests three possible interpretations (see p. 8 of the remand). It is clear from the plain language of the claim that the "promoter region" of the nucleic acid molecule within the cell must comprise SEQ ID NO: 1, but the claim does not set forth any functional language to describe what SEQ ID NO: 1 is doing within this promoter region. Thus, the Board suggests that the claim can be interpreted such that (1) SEQ ID NO: 1 contains a promoter region which does function in plant cells to cause production of an mRNA molecule, (2) that SEQ ID NO: 1 contains a "regulatory element" that acts in concert with a promoter region, for example SEQ ID NO: 1 is an enhancer, or (3) that SEQ ID NO: 1 is merely present within the construct as a "filler" sequence between the promoter region and a structural nucleic acid, and thus is part of the "promoter region" but imparts no function thereto.

The rejected claims also include claims 12-20 which are drawn to substantially purified nucleic acid molecules which comprise or consist of SEQ ID NO: 1 or a nucleic acid molecule that has a particular percent identity with SEQ ID NO: 1 (as little as 70% identity, with some claims requiring 100% identity).

The specification discloses over twenty thousand nucleic acid molecules that were isolated from the plant species *Glycine max*. The specification teaches that each one of these molecules may comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). There is no further guidance in the specification, however, to assist one in determining which of these possible characterizations is applicable to instant SEQ ID NO: 1. The specification provides only one specific reference to SEQ ID NO: 1 individually, on page 101 the specification teaches

that SEQ ID NO: 1 has 50% identity to a putative POL3 protein from *A. thaliana*. The specification does not, however, disclose what portion of this putative protein has identity with SEQ ID NO: 1. A sequence search by the examiner was unable to confirm this result. All other discussion in the specification of the potential function of the disclosed polynucleotide is generic in nature because it refers to all 20,082 nucleic acids disclosed in the specification in mass.

The specification teaches that the present invention includes "nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1 through SEQ ID NO: 20082 (p. 16)." Thus implying that a promoter region or a partial promoter region may be within SEQ ID NO: 1. The specification teaches that promoters "can include between about 300bp upstream and about 10kb upstream of the trinucleotide ATG sequence at the start site of a protein coding region (p. 16, final ¶)," and that "While in many circumstances a 300bp promoter may be sufficient for expression, additional sequences may act to further regulate expression (p. 17, 1st ¶)."

The specification does not provide any specific guidance as to whether SEQ ID NO: 1 comprises regulatory elements, sequence encoding polypeptides, introns, or intron/exon junctions. Given that the specification asserts that instant SEQ ID NO: 1 may include any or all of these, it is highly unpredictable based on the teachings of the specification as to whether or not instant SEQ ID NO: 1 contains or is a promoter element.

Turning to the three possible interpretations set forth by the Board of Appeals, the specification clearly supports the first possible interpretation. The specification further clearly suggests that the claimed molecules may encompass "regulatory elements" as discussed beginning on page 17 through page 24, which is the second interpretation. Regarding the third

interpretation, however, the specification does not ever appear to suggest the use of SEQ ID NO: 1 or any of the disclosed nucleic acids to "serve as a filler sequence between the promoter region and a structural nucleic acid molecule," and thus this potential interpretation of the claimed invention does not appear to be applicable to the instant claims, when the claims are interpreted in light of the specification.

The specification does not exemplify the use of SEQ ID NO: 1 attached to or within a promoter construct. Regarding the potential function of SEQ ID NO: 1, the specification does not provide any specific teaching. The specification discloses over twenty thousand nucleic acid molecules that were isolated from the plant species *Glycine max*. The specification teaches that each one of these molecules may comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). The specification teaches that the present invention includes "nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1 through SEQ ID NO: 20082 (p. 16)." Thus implying that a promoter region or a partial promoter region may be within SEQ ID NO: 1. However, since all assertions of the function of SEQ ID NO: 1 are given generally for this sequence and over twenty thousand other sequences, none of these statements can be considered specific to SEQ ID NO: 1. Further, the different statements conflict, as it is highly unlikely that the single 394 base pair fragment of SEQ ID NO: 1 at the same time comprises regulatory elements, structural genes, intron and promoter regions.

Thus, given the instant specification, it is highly unpredictable how to use instant SEQ ID NO: 1 as part of an exogenous promoter region as set forth in claims 1 and 7. First, while the

specification suggests that SEQ ID NO: 1 may contain a promoter or a partial promoter, the specification suggests with equal specificity that SEQ ID NO: 1 may contain a structural gene encoding a protein, that SEQ ID NO: 1 may contain an intron, and that SEQ ID NO: 1 may contain and intron/exon boundary. Thus, it is left to one attempting to make and use the claimed products to determine which instant SEQ ID NO: 1 actually is and how it can be used within the constructs claimed. Even given the choice between the suggestion that SEQ ID NO: 1 comprises a promoter or a partial promoter, the specification does not provide any guidance or suggestion as to which is the case for SEQ ID NO: 1. This is an important distinction since the entire functioning of a promoter is entirely sequence specific. For example, if SEQ ID NO: 1 contained only a partial promoter, it is highly unpredictable as to whether or not that partial promoter would function to promote production of an mRNA or which part of SEQ ID NO: 1 is in fact the "promoting" part since one cannot simply look at SEQ ID NO: 1 and identify these regions by any disclosed sequence characteristics, and since the function of a promoter is highly sequence specific. Or, if SEQ ID NO: 1 contains a regulatory element, it is highly unpredictable how that element would function in view of the fact that there are hundreds of possible regulatory functions known, and there is no known way to predict if one of these is attributable to instant SEQ ID NO: 1. For example, the instant specification provides a seven page listing of possible functions that any potential regulatory element contained within the disclosed sequences might have (specification pages 17-23). Each function would warrant use in a different type of system for expression under different circumstances to achieve an effect specific to the regulatory element. For example, the specification makes reference to oxygen responsive elements, light regulatory elements, and elements responsive to gibberellin. In order to make the claimed

invention, one would have to undertake enormous amounts of experimentation to discover if in fact SEQ ID NO: 1 is a promoter or comprises a promoter or a regulatory element, as suggested by the claims and also suggested by the specification, or if SEQ ID NO: 1 contains a structural gene as also suggested by the specification, or if SEQ ID NO: 1 comprises an intron or an intron/exon boundary as also suggested by the specification.

Considering then, the state of the prior art, instant SEQ ID NO: 1 is a novel sequence. A sequence search by the examiner in a variety of nucleic acid databases did not identify any sequence in the prior art with greater than 29% identity over the full length of SEQ ID NO: 1. For example, GenBank AF147259 (13 August 1999) provides the sequence of an A. thaliana BAC, and nucleotides 46185-46519 of this sequence have 29% identity with instant SEQ ID NO: 1. This however is an uncharacterized portion of nucleic acid, and even if the homology were exact would not provide any further guidance as to whether instant SEQ ID NO: 1 contains a promoter or promoter elements, or an intron, or a coding sequence.

Furthermore, even if SEQ ID NO: 1 contains a functioning promoter or regulatory element, with regard to claims 12-15, the prior art makes clear that the ability of a promoter to function is highly sequence specific. The art teaches repeatedly that mutations in a critical region of a promoter element can destroy the ability of a construct to function in promotion. For example, Pietrzkowski *et al.* (Experimental Cell Research, 193, 283-290 (1991)) teaches that when synthetic promoters were produced wherein the sequence of an enhancer element was mutated, little to no promotion was observed from the constructs where the promoter was mutated (see for example Figure 6). Chan *et al.* (Plant Molecular Biology 46 :131-141, (2001)) teach that mutation in a critical XXIII element of the GAPB promoter abolished transcription

completely (Figure 6), while mutations in other elements did not abolish activity (Figure 6). Thus, it is evident that it is highly unpredictable how promoter elements will respond to even very minor sequences changes. In addition, the order in which promoter elements occur in a construct has an effect on the functionality of the promoter. Omilli *et al.* (Molecular and Cellular Biology, June 1986, p. 1875-1885) teach that the relative arrangement of promoter elements is a critical factor contributing to the activity of the promoter (ABSTRACT, for example).

Thus, having considered the scope of the claims, the teaching in the specification, the guidance in the prior art, the lack of working examples, and the high level of unpredictability with respect to the prior art, it is concluded that it would require undue experimentation to make and use the claimed invention.

(10) Response to Argument

Claims Interpretation

Regarding the scope of claims 3, 5, 6, 7, 9, and 10, the remand by the board suggests three possible interpretations (see p. 8 of the remand dated 5/23/05). It is clear from the plain language of the claim that the "promoter region" of the nucleic acid molecule within the cell must comprise SEQ ID NO: 1, but the claim does not set forth any functional language to describe what SEQ ID NO: 1 is doing within this promoter region. Thus, the Board suggests that the claim can be interpreted such that (1) SEQ ID NO: 1 contains a promoter region which does function in plant cells to cause production of an mRNA molecule, (2) that SEQ ID NO: 1 contains a "regulatory element" that acts in concert with a promoter region, for example SEQ ID NO: 1 is an enhancer, or (3) that SEQ ID NO: 1 is merely present within the construct as a

"filler" sequence between the promoter region and a structural nucleic acid, and thus is part of the "promoter region" but imparts no function thereto.

It is well settled that the claims must be given their broadest reasonable interpretation in view of the specification.

The specification discloses over twenty thousand nucleic acid molecules that were isolated from the plant species *Glycine max*. The specification teaches that each one of these molecules may comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). There is no further guidance in the specification, however, to assist one in determining which of these possible characterizations is applicable to instant SEQ ID NO: 1. The specification provides only one specific reference to SEQ ID NO: 1 individually, on page 101 the specification teaches that SEQ ID NO: 1 has 50% identity to a putative POL3 protein from *A. thaliana*. The specification does not, however, disclose what portion of this putative protein has identity with SEQ ID NO: 1. A sequence search by the examiner was unable to confirm this result. All other discussion in the specification of the potential function of the disclosed polynucleotide is generic in nature because it refers to all 20,082 nucleic acids disclosed in the specification in mass.

The specification teaches that the present invention includes "nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1 through SEQ ID NO: 20082 (p. 16)." Thus implying that a promoter region or a partial promoter region may be within SEQ ID NO: 1. The specification teaches that promoters "can include between about 300bp upstream and about 10kb upstream of the trinucleotide ATG sequence at the start site of a protein coding region (p. 16, final ¶)," and that "While in many

circumstances a 300bp promoter may be sufficient for expression, additional sequences may act to further regulate expression (p. 17, 1st ¶)."

The specification does not provide any specific guidance as to whether SEQ ID NO: 1 in particular comprises regulatory elements, sequence encoding polypeptides, introns, or intron/exon junctions. Given that the specification asserts that instant SEQ ID NO: 1 may include any or all of these, but fails to even positively identify a single one of these suggested elements within SEQ ID NO: 1, it cannot be definitely determined if SEQ ID NO: 1 actually contains a promoter or not, based on the teachings of the specification.

Turning to the three possible interpretations set forth by the Board of Appeals, the specification clearly supports the first possible interpretation. The specification further clearly suggests that the claimed molecules may encompass "regulatory elements" as discussed beginning on page 17 through page 24, which is the second interpretation. Regarding the third interpretation, however, the specification does not ever appear to suggest the use of SEQ ID NO: 1 or any of the disclosed nucleic acids to "serve as a filler sequence between the promoter region and a structural nucleic acid molecule," and thus this potential interpretation of the claimed invention does not appear to be applicable to the instant claims, when the claims are interpreted in light of the specification. The board's remaining comments are addressed in the rejections in this Examiner's Action.

Answer to Traversal

Appellant states that they have confirmed a specific utility of SEQ ID NO: 1 by conducting a BLASTN analysis, namely stating that "The results of a BLASTN analysis of SEQ ID NO: 1 show that SEQ ID NO: 1 has 95 percent identity to a sequence obtained *from Glycine*

max (soybean) (p. 6 of the brief)." Instant SEQ ID NO: 1 is 394 nucleotides long, and the alignment provided in the response to final shows that there is a 95% identity over a stretch of 105 nucleotides. The identity, therefore, is not over the full length of SEQ ID NO: 1, nor does it appear that it is the full length of the molecule in the database which it appears from the limited data given in Appellant's papers is 611 nucleotides (see page 2 of the paper received 1/30/07). The data given from appellant's search is not complete since the full length alignment of the two sequences is not given, nor are the parameters of the BLASTN search given. It is clear from Appellant's paper that the alignment is not over the full length of the sequence given in the database, since both molecules involved are substantially longer than the aligned region. Appellant did not provide the database record of the nucleic acid with identity to SEQ ID NO: 1 for the examiner's consideration. The assertions in the remarks, therefore, fail to provide any substantial evidence for the examiner to consider and amount only to attorney arguments. Attorney arguments cannot replace proper evidence on the record. Appellant is reminded that any evidence filed in the application must be appropriately timely filed for consideration by the examiner. Furthermore, there is no suggestion or evidence on the record that the sequence relied upon by applicant to assert this supposed utility was available at the time the invention was filed, and even further still, this potential utility is not asserted in the specification and so, there is no nexus between the assertion in the arguments and the teachings in the specification.

Appellant states that given the identity between SEQ ID NO: 1 and the claimed molecules, SEQ ID NO: 1 has a specific utility (page 6 of the brief). The remarks do not address why the fact that a portion of SEQ ID NO: 1 might have identity with a portion of a molecule that is expressed in roots of soybean plants challenged with the bacteria *B. japonicum* would

impart utility on a transformed cell or transformed plant that contains SEQ ID NO: 1 as part of an exogenous promoter region. Regarding the claims to isolated nucleic acid molecules, Appellant states that SEQ ID NO: 1 can be used to isolate genes, map genes, and determine gene function associated with nitrogen fixation because it is well known that *B. japonicum* is a gram negative, nitrogen-fixing bacterium belonging to the Rhizobiaceae family. This potential utility is not set forth in the specification, therefore, it is not an asserted utility provided at the time of filing of the application. Even if it were, however, the research suggested by applicant is simply a suggestion to undertake further experimentation to see if instant SEQ ID NO: 1 is possibly related to nitrogen fixation in soybean. Since the identity stated is only over a portion of the claimed molecule, and the molecule in the GenBank record, it is not sufficient to conclude that these two molecules are even functionally related.

Appellant states on page 7 of the brief that they have set forth a specific, substantial, and well-established utility for SEQ ID NO: 1, and by extension for the transformed plant cell and transformed plant comprising SEQ ID NO: 1 based upon the identity of SEQ ID NO: 1 with the molecule referred to in the GenBank record. This assertion is not given in the specification, and there is no indication on the record that the sequence relied upon by Appellant was in GenBank database as of the effective filing date for the instantly claimed invention. Even if the sequence were available, there is no showing that SEQ ID NO: 1 itself is differentially expressed in response to challenge by the bacteria. Approximately one quarter of SEQ ID NO: 1 has identity with less than twenty percent of the full length molecule that is disclosed in the GenBank record. There is no guidance in the specification as to which portion of SEQ ID NO: 1 has identity with the molecule in the GenBank record. While hybridization of SEQ ID NO: 1 might have pulled

up the molecule in the GenBank record from a soybean nucleic acid sample, it likely would have also resulted in the isolation of an entire population of molecules since low stringency conditions would have to be used to pull up the molecule in the GenBank record give the low percentage of the two sequences that actually share the identity. Even knowing that these two molecules share a portion of identity does not tell one of skill in the art that SEQ ID NO: 1 itself is involved in nitrogen fixation, or even that it is differentially expressed in response to challenge with the bacteria. Further, the potential utilities asserted in the brief were not well-established at the time of filing, indeed, there is no evidence on the record that the molecule disclosed in the GenBank record referred to in the arguments was even disclosed prior to the effective filing date of the claimed invention.

Appellant did not assert or contemplate in the specification any specific utility for instant SEQ ID NO: 1, or that it might be expressed in root hair challenged with the bacteria *B. japonicum*. Therefore, one cannot deduce based on the teachings of the specification that Appellant had any evidence that the claimed nucleic acid was expressed in root hair challenged with the bacteria *B. japonicum* or that SEQ ID NO: 1 had any identity to such a molecule such that it could be used to isolate such a molecule. Appellant's potential showing that post-filing one could have compared the claimed molecule to a post-filing disclosure to determine a potential utility for the claimed invention is immaterial, since Appellant is required to disclose their invention and Appellant did not provide any evidence that he contemplated that his claimed nucleic acid is expressed in root hair challenged with the bacteria *B. japonicum*. An artisan would have had to carry out further characterization of the nucleic acid and constructs that are claimed to determine that the claimed nucleic acid was so expressed and such characterization is

considered further research and therefore cannot provide a specific and substantial asserted utility.

Appellant's further analysis to establish that the claimed molecule has identity with a later discovered molecule exemplifies that the application AS FILED was an invitation to one of skill in the art to undertake further analysis to attempt to establish a specific and substantial utility for the claimed invention. A rejection for lack of utility cannot be rebutted by relying on a utility that would have not been readily apparent at the time the application was filed. Applicant filed an application in which over twenty thousand different nucleic acid sequences were disclosed, all identified as having the same potential utilities, and it was not apparent from reading the specification that SEQ ID NO: 1 has a small portion which has high identity to a small portion of another molecule that is expressed in root hair challenged with the bacteria *B. japonicum*. If Appellant desires to rely on the fact that SEQ ID NO: 1 has this identity to the molecule disclosed in the GenBank record to establish the utility of the claimed invention, then the specification is incomplete (MPEP 608.01(p)). The MPEP states "A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which the invention pertains to make and use the invention as of its filing date. In re Glass, 492 F.2d 1228, 181 USPQ 31 (CCPA 1974). While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques, where necessary, as to enable those persons skilled in the art to make and utilize the invention." There is no assertion or even hint in the specification that the claimed polynucleotide has a portion which shared 95% identity with a portion of a molecule that is expressed in root hair challenged with the bacteria *B.*

japonicum, yet in these remarks Appellant is asserting that it is this fact which gives utility to the claimed molecule. It appears the specification as filed is incomplete.

Appellant points out on page 8 of the brief that the "Office must accept a stated utility by an applicant unless the Office has evidence or sound scientific reasoning to rebut the applicant's assertion." This is true when a substantial, specific and credible asserted utility is provided in the specification. In this case, as discussed in the rejection, there are no specific and substantial utilities given in the specification.

Appellant points out on page 9 of the brief that the specification disclosing isolation and mapping of genes and determining gene function associated with molecules of the invention as a stated utility for the molecules of the invention, and that nitrogen fixation is merely an example of such a utility. Nitrogen fixation is an example of the utility that was not asserted in the specification. appellant points out that the MPEP states that the specification need not disclose what is well known in the art or already available to the public. The proposed utility relied upon by Appellant was not well known in the art or already available to the public at the time the invention was made. The rejection is maintained.

Appellant traverses the lack of enablement rejection which follows the rejection for lack of utility on the same grounds as the traversal for the lack of utility rejection under 101. For the reasons previously stated in this Examiner's Answer, the rejection is maintained.

Appellant traverses the lack of enablement rejection beginning on page 11 of the brief. Appellant states that performing routine and well-known steps cannot create undue experimentation even if the steps are laborious. However, in this case, the steps are not merely routine. First, one would have to establish what function the claimed molecules can be assigned:

are they promoter molecules, enhancer molecules, introns, coding sequences, or are all of these elements present at different portions of SEQ ID NO: 1? Without this information, it is impossible to predict how SEQ ID NO: 1 can be modified and still retain the same function it currently has. Appellant states that the art area in this case is neither unpredictable nor undeveloped. The examiner has discussed the level of unpredictability in this technology in the rejection. The examiner disagrees with Appellant and supports her position in the rejection that the unpredictability of modifying sequences and retaining function is quite high.

Appellant points out that only up to 118 nucleotides in SEQ ID NO: 1 can be modified within the scope of the claims. Agreed.

Appellant argues that this number vastly over-counts the number of possible changes because the specification teaches that conservative substitutions generally retain functionality while non-conservative substitutions generally do not. There is no requirement in the claim that only conservative substitutions be made. Even if there were, this would be meaningless since it is not disclosed whether or not SEQ ID NO: 1 encodes a polypeptide. The specification teaches that the disclosed SEQ ID NO: 1 may comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). The specification does not provide any specific guidance as to whether SEQ ID NO: 1 in particular comprises regulatory elements, sequence encoding polypeptides, introns, or intron/exon junctions. Given that the specification asserts that instant SEQ ID NO: 1 may include any or all of these, but fails to even positively identify a single one of these suggested elements within SEQ ID NO: 1, it cannot be definitely determined if SEQ ID NO: 1 actually contains a promoter or not, based on the teachings of the specification. If SEQ ID NO: 1 does

not comprise a sequence encoding a polypeptide, then the discussion of conservative substitutions is misplaced, since such a conversation is not relevant to the function of regulatory elements, introns, or intron/exon junctions.

Appellant asserts that the issue is whether one of ordinary skill in the art can reasonably predict what the effects of substitutions on SEQ ID NO: 1 would be. Without knowing the function of SEQ ID NO: 1, one cannot predict how that function might change with any substitution, conservative or not.

(11) Related Proceeding(s) Appendix

Copies of the court or Board decision(s) Ex parte Fischer and In re Fisher, identified in the Related Appeals and Interferences section of this examiner's answer are provided attached to the Appeal Brief dated 5/25/07.

No decision has been rendered in 09/684016, 10/361942, 10/199129, 09/920953, 09/237183, 09/692257, 10/437963, or 09/531113, and so no decision is provided.

Prosecution has been reopened in 09/663423.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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